Pramipexole and Compulsive Masturbation

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ABSTRACT

Objective: Exploration of a possible relationship between pramipexole and compulsive masturbation.

Methods: We present a case report.

Results: Given the temporal overlap between pramipexole prescription and its discontinuation, and the onset and cessation of the patient's hypersexual behavior, there appears to be a strong likelihood of association.

Conclusions: Like other dopamine agonists, pramipexole may precipitate compulsive behaviors, including hypersexual behavior in the form of compulsive masturbation.

INTRODUCTION

Pramipexole is a non-ergot dopamine agonist that binds to D_2 and D_3 dopamine receptors in the striatum and substantia nigra. This drug is a full dopamine agonist (bromocriptine and pergolide are partial agonists) and is more selective for the D_3 receptor than either bromocriptine or pergolide. Pramipexole has no significant effects on adrenergic or serotonergic receptor sites and is primarily prescribed for the treatment of Parkinson's disease and restless legs syndrome.

In the empirical literature, there are a number of reports of compulsive

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behaviors in association with dopamine agonist therapy. For example, there are several case reports of dopamine agonist therapy and pathological gambling.[1-9] In one series of 388 patients, 4.4 percent developed pathological gambling.[2] In a sample of Italian patients, the prevalence of pathological gambling was 6.1 percent, compared with 0.25 percent among controls.[3]

In addition to pathological gambling, other compulsive behaviors have been reported with the use of dopamine agonists. For example, there are several case reports of patients compulsively using dopamine agonist drugs, a phenomenon that is identified as "dopamine dysregulation syndrome"[10] or "hedonistic homeostatic dysregulation."[11] Pezzella and colleagues describe this behavior as "self-medication and addiction to dopaminergic drugs."[11] Punding, a stereotypic behavior characterized by the repetitive handling and examination of mechanical objects, has also been reported in association with dopamine agonist therapy.[12,13] In one case, punding manifested as "computer addiction."[13] There have also been case reports of compulsive eating with dopamine agonist therapy.[14]

Although infrequently reported, hypersexual behavior has also been described in patients on dopamine agonists. Weintraub and colleagues found that 2.6 percent of their patient series reported compulsive sexual behaviors while on dopamine agonist therapy.[7] In their discussion of findings, the authors never explicitly describe these behaviors. However, pramipexole was the most frequently implicated drug. In a retrospective review of medical records, Klos and colleagues described 15 cases of hypersexuality associated with dopamine agonist therapy.[15] These hypersexual behaviors included the compulsive use of pornography, extramarital affairs, and delusions of spouse infidelity. One-third of the patients were prescribed pramipexole.

While all dopamine agonists are generally associated with diverse compulsive behaviors, some investigators believe that pramipexole is more likely to be causative.[8,9] Some studies support this suspicion. For example, while the precise neurophysiology of this association remains unknown, rats treated chronically with a D_2/D_3 agonist developed compulsive checking of specific locations.[16] By being a full and selective D_3 agonist, pramipexole may pose a heightened risk for the development of compulsive behaviors. These behaviors may be mediated through ventral-striatal over-stimulation, and manifest as novelty and reward-seeking.[17] While compulsive behaviors associated with dopamine agonists may appear to have overtones of obsessive-compulsive disorder, comparative examination does not appear to support a relationship between the two.[18]

In the following case report, we describe a male patient who was treated with pramipexole for restless legs syndrome. While on treatment with dopamine agonist therapy, he developed relentless compulsive masturbation.

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CASE REPORT

Mr. T. was a 67-year-old white man with medical diagnoses of hypertension, complex-partial epilepsy, liver cancer (status-post resection), hemochromatosis, gastroesophageal reflux, sleep apnea, restless legs syndrome, and major depression. His medications were lisinopril 10mg daily, clonidine transdermal 0.2mg daily, amlodipine 10mg daily, oxcarbazepine 600mg twice per day, clopidogrel 75mg daily, allopurinol 100mg daily, aspirin daily, hydrochlorothiazide 25mg daily, ranitidine 75mg daily, pramipexole 0.5mg at bedtime, and escitalopram 10mg daily.

During an appointment, Mrs. T. voiced her concern about her husband's hypersexuality. She stated that for the past 3 to 4 years, Mr. T. had experienced a very high libido and was masturbating approximately 6 to 8 times a day. Mrs. T. explained that he would also wake her up in the middle of the night to satisfy his needs. In addition, he would excuse himself from the dinner table at home, in restaurants, or at the homes of friends to masturbate. The patient acknowledged these behaviors but was unable to explain them. Upon careful inquiry, the patient affirmed that his symptoms began shortly after starting pramipexole for restless legs syndrome. A literature search indicated a possible relationship between compulsive behaviors and pramipexole, and the temporal association was convincing. The patient was advised to discontinue the pramipexole. Mr. T. and his wife returned for a follow-up encounter two weeks later and indicated that since the discontinuation of the pramipexole, there had been a marked decrease in his masturbatory behavior, which was no longer daily.

CONCLUSIONS

It appears that dopamine agonists may, in susceptible patients, result in various types of compulsive behaviors. We have previously discussed some possible neurophysiological substrates that may account for these unusual behaviors. However, a number of

questions remain unanswered. For example, are there specific dopamine subreceptors that, when stimulated, are more likely to cause compulsive behaviors (e.g., D_3 receptors)? Will the various dopamine agonists evidence differing rates of risk for compulsive behaviors based upon their dopamine receptor profiles? Are there any predisposing factors in the patient's premorbid history that partially account for the specific type of compulsive behavior manifested? Only further investigation will clarify these intriguing issues. For the time being, however, it seems prudent to recommend that clinicians who see patients on dopamine agonists routinely inquire about the unusual side effect of compulsive behavior, including hypersexuality and masturbation. In addition, these drugs should be used very cautiously and with great discretion in sex offenders.

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